

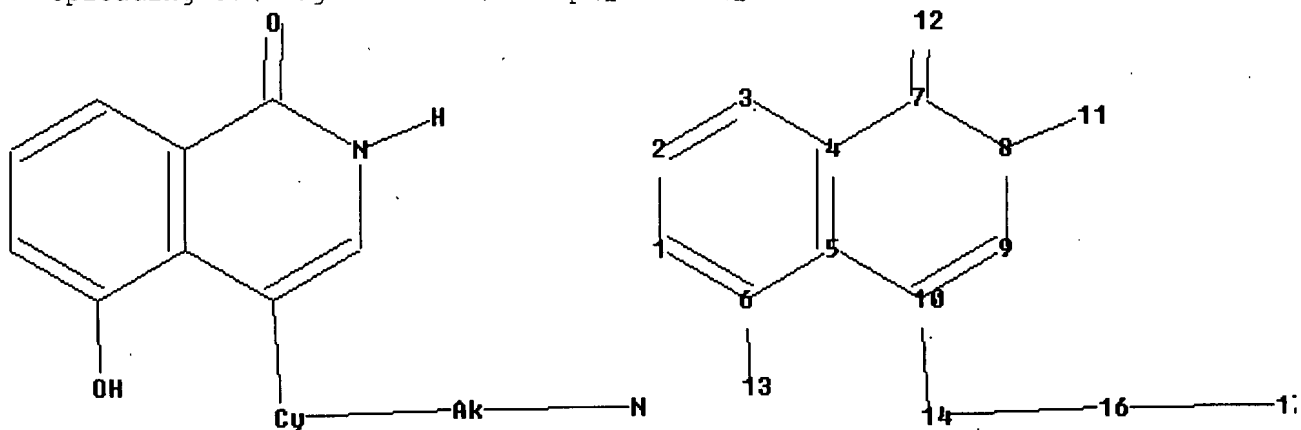
10/521,565

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***** STN Columbus *****

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chain nodes :

11 12 13 14 16

ring nodes :

1 2 3 4 5 6 7 8 9 10

ring/chain nodes :

17

chain bonds :

6-13 7-12 8-11 10-14 14-16 16-17

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10

exact/norm bonds :

4-7 5-10 6-13 7-8 7-12 8-9 9-10 10-14 14-16 16-17

exact bonds :

8-11

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:CLASS 12:CLASS 13:CLASS 14:Atom 16:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> s l1 sam

L2 1 SEA SSS SAM L1

=> s l1 full

L3 144 SEA SSS FUL L1

=> file caplus

=> s 13

L4 3 L3

=> s 14 and pd< july 2002

22724470 PD< JULY 2002

(PD<20020700)

L5 0 L4 AND PD< JULY 2002

=> dis 14 1-3 bib abs fhitr

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1137938 CAPLUS Full-text

DN 144:45339

TI Neuroprotective effects of KCL-440, a new poly(ADP-ribose) polymerase inhibitor, in the rat middle cerebral artery occlusion model

AU Ikeda, Yasuhiko; Hokamura, Kazuya; Kawai, Tomoyuki; Ishiyama, Junichi; Ishikawa, Kumi; Anraku, Tsuyoshi; Uno, Takashi; Umemura, Kazuo

CS Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 432-8014, Japan

SO Brain Research (2005), 1060(1-2), 73-80

CODEN: BRREAP; ISSN: 0006-8993

PB Elsevier B.V.

DT Journal

LA English

AB It is reported that ischemic brain injury is mediated by the activation of poly(ADP-ribose) polymerase (PARP). In this study, we examined the pharmacol. profile of KCL-440, a new PARP inhibitor, and its neuroprotective effects in the rat acute cerebral infarction model induced by photothrombotic middle cerebral artery (MCA) occlusion. In an in vitro study, KCL-440 exhibited potency with regard to inhibition of PARP activity, with an IC50 value of 68 nM. An in vivo pharmacokinetic study showed that the brain concentration of KCL-440 was sufficient to inhibit PARP activity during the i.v. infusion of KCL-440 at the rate of 1 mg/kg/h. KCL-440 at various doses or saline was administered for 24 h immediately after the MCA occlusion. Administration of KCL-440 led to a dose-dependent reduction in the infarct size at 24 h after MCA occlusion. Infarct sizes were $44.8\% \pm 3.0\%$ (n = 8), $40.5\% \pm 1.1\%$ (n = 8), $38.2\% \pm 1.4\%$ (n = 8), $35.1\% \pm 2.1\%$ (n = 8), $34.2\% \pm 2.3\%$ (n = 7), $32.6\% \pm 1.9\%$ (n = 8), and $31.0\% \pm 2.1\%$ (n = 5) at doses of 0, 0.01, 0.03, 0.1, 0.3, 1.0, and 3.0 mg/kg/h. When compared to the control group, a statistically significant difference was observed in the doses that were higher than 0.03 mg/kg/h. When the infusion of KCL-440 (1 mg/kg/h, n = 8) was started at 1 h after the MCA occlusion, a significant reduction in infarct size was observed; this was not observed when KCL-440 infusion was started 2 or 3 h after the MCA occlusion. Furthermore, increased poly(ADP-ribose) immunostaining was confirmed at the ischemic border zone 2 h after the MCA occlusion, and it was reduced by KCL-440 treatment. These results suggest that KCL-440 is a possible neuroprotective agent with high blood-brain barrier permeability and high PARP inhibitory activity.

IT 651029-09-3, KCL 440

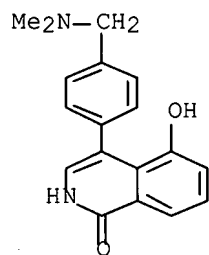
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(neuroprotective effects of KCL-440, a new poly(ADP-ribose) polymerase inhibitor, in the rat middle cerebral artery occlusion model)

RN 651029-09-3 CAPLUS

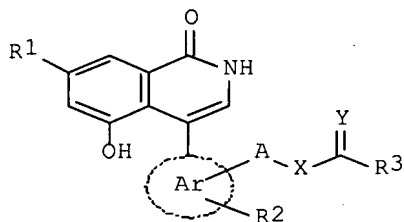
CN 1(2H)-Isoquinolinone, 4-[4-[(dimethylamino)methyl]phenyl]-5-hydroxy- (CA INDEX NAME)



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:252487 CAPLUS Full-text
DN 140:287279
TI Preparation of 4-(substituted aryl)-5-hydroxyisoquinolinone derivatives as
poly(ADP-ribose) polymerase inhibitors
IN Shiga, Futoshi; Kanda, Takahiro; Takano, Yasuo; Ishiyama, Junichi
PA Kyorin Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004024694	A1	20040325	WO 2003-JP11346	20030905
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003264386	A1	20040430	AU 2003-264386	20030905
PRAI	JP 2002-263918	A	20020910		
	WO 2003-JP11346	W	20030905		
OS	MARPAT 140:287279				
GI					



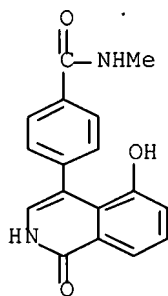
I

AB Title compds. I (R1 = H, halo; R2 = H, halo, OH, alkyl, haloalkyl, alkoxy, haloalkoxy; Ar = Ph, naphthyl, heteroaryl, etc.; A = bond, alkylene; X = bond, O, amino; Y = O, S; R3 = amino, etc) and their pharmacol. acceptable salts, useful as poly(ADP-ribose) polymerase inhibitors, are prepared 1,2-Dihydro-5-hydroxy-4-[4-(N-methylcarbamoyl)phenyl]-1-oxoisoquinoline was prepared and showed inhibitory activity against PARP with IC50 of 144 n mol/L.

IT 675577-26-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of 4-(substituted aryl)-5-hydroxyisoquinolinone derivs. as poly(ADP-ribose) polymerase inhibitors)

RN 675577-26-1 CAPLUS

CN Benzamide, 4-(1,2-dihydro-5-hydroxy-1-oxo-4-isoquinolinyl)-N-methyl- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:80658 CAPLUS Full-text

DN 140:146017

TI Preparation of hydroxyisoquinolinone derivatives as poly(ADP-ribose) polymerase inhibitors

IN Shiga, Futoshi; Kanda, Takahiro; Kimura, Tetsuya; Takano, Yasuo; Ishiyama, Junichi; Kawai, Tomoyuki; Anraku, Tsuyoshi; Ishikawa, Kumi

PA Kyorin Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 151 pp.
 CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009556	A1	20040129	WO 2003-JP9332	20030723
	WO 2004009556	A9	20041021		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

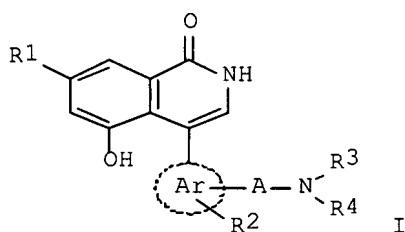
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2493234	A1	20040129	CA 2003-2493234	20030723
AU 2003255149	A1	20040209	AU 2003-255149	20030723
EP 1544194	A1	20050622	EP 2003-765364	20030723

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1671668	A	20050921	CN 2003-817589	20030723
NZ 537793	A	20070531	NZ 2003-537793	20030723
US 2006173039	A1	20060803	US 2005-521565	20050119
MX 2005PA00983	A	20050818	MX 2005-PA983	20050124

PRAI JP 2002-214673 A 20020724
 WO 2003-JP9332 W 20030723
 OS MARPAT 140:146017
 GI



AB Title compds. I (ring Ar = Ph, naphthyl, 5- or 6-membered heteroaryl, R1 = H, halo; R2 = H, halo, OH, alkyl, aryl, etc.; R3, R4 = H, halo, etc; A = alkylene, alkenylene) and their pharmacol. acceptable salts, useful as poly(ADP-ribose) polymerase (PARP) inhibitors, are prepared. Thus, 1,2-dihydro-4-[4-(dimethylaminomethyl)phenyl]-5-hydroxy-1-oxoisoquinoline was prepared and showed inhibition of PARP with IC50 of 30 nM.

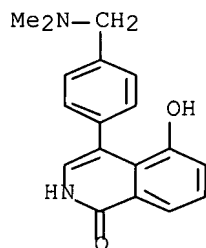
IT 651029-09-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of hydroxyisoquinolinone derivs. as poly(ADP-ribose) polymerase inhibitors)

RN 651029-09-3 CAPLUS

CN 1(2H)-Isoquinolinone, 4-[4-[(dimethylamino)methyl]phenyl]-5-hydroxy- (CA INDEX NAME)



10/521,565

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL LOGOFF AT 17:05:14 ON 08 NOV 2007